HIGH PRODUCTION VOLUME (HPV) CHALLENGE PROGRAM

Test Plan for 2-Pentanamine, 2,4,4-trimethyl- (Primene™ TOA) CAS Number 107-45-9

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TABLE OF CONTENTS

OVERVIEW

The Rohm and Haas Chemicals, LLC hereby submits for review and public comment the test plan for 2-Pentanamine, 2,4,4-trimethyl- (Primene™ TOA) (CAS Number 107-45-9) under the Environmental Protection Agency's (EPA) High Production Volume (HPV) Chemical Challenge Program. Here we provide existing data on 2-Pentanamine, 2,4,4-trimethyl-, and list additional testing to be performed to adequately fulfill the Screening Information Data Set (SIDS) for physico-chemical, environmental fate, ecotoxicity and human health effects endpoints.

2-Pentanamine, 2,4,4-trimethyl- (Primene™ TOA) is a strong base, C_8 primary amine in which the nitrogen atom is linked to a tertiary carbon atom. Primene™ TOA is used primarily as an intermediate for making salts and derivatives. Many applications of Primene™ TOA result from its unique physical and chemical properties which differ markedly from those of related straight-chain or less branched isomers. It is a mobile liquid at ambient temperature and maintains its low viscosity down to very low temperatures. Primene™ TOA is much more soluble in petroleum solvents than analogous less branched amines. These advantageous properties are thought to arise from its highly branched structure and a low tendency toward crystallization. In addition, it shows outstanding color stability because of its high resistance to oxidation.

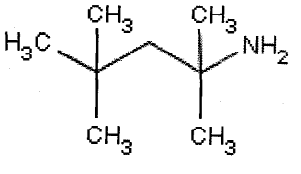
New and additional testing is required to fulfill the SIDS endpoints. A testing program has been designed with the intention of satisfying these requirements.

GENERAL INFORMATION

CAS Number: 107-45-9

Molecular Weight: 129

Structure and Formula: $C_8H_{19}N$



TEST PLAN SUMMARY

CAS No. 107-45-9	Information	OECD Study	Estimation	GLP	Acceptable	New Testing Required
Study	Y/N	Y/N	Y/N	Y/N	Y/N	Y/N
Physical/Chemical Data						
Melting Point	N	-	-	-		Y
Boiling Point	N	-	-	-	-	Y
Density	Y	N	-	N	Y	N
Vapor Pressure	N	-	-	-	-	Y
Partition Coefficient	Y	N	-	N	Y	N
Water Solubility	N	-	-	-	-	Y
Dissociation Constant (pH and pKa Values)	Y	N	-	N	Y	N
Other P/C Studies						
Flash Point	Y	N	-	N	Y	-
Pour Point	Y	N	-	N	Y	-
Surface Tension/Interfacial Tension with Water	Y	N	-	N	Y	-
Environmental Fate and Pathway						
Photodegradation	Y	-	Y	-	Y	N
Stability in Water (Hydrolysis)	Y	-	-	-	-	N
Transport and Distribution (Fugacity)	Y	-	Y	-	Y	N
Biodegradation	N	-	-	-	-	Y
Ecotoxicity						
Acute Toxicity to Fish	N	-	-	-	-	Y
Acute Toxicity to Daphnia	N	-	-	-	-	Y
Toxicity to Algae	N	-	-	-	-	Y
Toxicity						
Acute Oral	Y	Y	-	Y	Y	N
Repeated Dose	N	-	-	-	-	Y
Genetic Toxicity in vitro						
Gene Mutation	Y	Y	-	Y	Y	N
Genetic Toxicity in vivo	N	-	-	-	-	Y
Reproduction Toxicity	N	-	-	-	-	Y
Development/Teratogenicity	N	-	-	-	-	Y
Human Experience	N	-	-	-	-	-
Other Toxicity Studies						
Skin Irritation	Y	Y	-	Y	Y	-
Eye Irritation	Y	-	-	-	Y	-

TEST PLAN DESCRIPTION FOR EACH SIDS ENDPOINT

A. Physicochemical

Melting Point- This endpoint will be tested using OECD 102 to fill the SIDS requirement.

Boiling Point- This endpoint will be tested using OECD 103 to fill the SIDS requirement.

Density- A value for this endpoint was determined using an Anton-Paar DMA-46 densitometer at the Analytical Research Department of the Rohm and Haas Company in Spring House, PA. No data on whether the test was conducted in compliance with GLP, but was reviewed internally and has been deemed valid.

Vapor Pressure- This endpoint will be tested using OECD 104 to fill the SIDS requirement.

Partition Coefficient- A value for this endpoint was determined from analyses that followed the Shake Flask Method. This test was not conducted in compliance with GLP, but was reviewed internally and has been deemed valid.

Water Solubility- This endpoint will be tested using OECD 105 to fill the SIDS requirement.

Dissociation Constant- A value for this endpoint was determined by Potentiometric titration to measure the Half Neutralization Potential (HNP). From this result a pKa value was estimated. This test was not conducted in compliance with GLP, but was reviewed internally and has been deemed valid.

Conclusion- Testing will be conducted to satisfy those SIDS endpoints which have not been filled.

B. Environmental Fate and Pathway

Photodegradation- This endpoint is satisfied by estimation.

Stability in Water- It was attempted to satisfy this endpoint by estimation.

Transport and Distribution- This endpoint is satisfied by estimation.

Biodegradation- This endpoint will be tested using OECD 301B to fill the SIDS requirement.

Conclusion- No data for these endpoints exists. Modeling/estimation was conducted to satisfy the photodegradation, hydrolysis and fugacity endpoints. Testing will be conducted to satisfy the biodegradation endpoint.

C. Ecotoxicity Data

Acute Toxicity to Fish- This endpoint will be tested using OECD 203 to fill the SIDS requirement.

Acute Toxicity to Aquatic Invertebrates- This endpoint will be tested using OECD 202 to fill the SIDS requirement.

Acute Toxicity to Aquatic Plants- This endpoint will be tested using OECD 201 to fill the SIDS requirement.

Conclusion- No data for these endpoints exists. Testing will be carried out according to the applicable OECD guidelines.

D. Toxicological Data

Acute Toxicity- This endpoint is filled by data from a study assessing toxicity following oral exposure. Acute oral toxicity was evaluated in male and female rats. In addition, a study was conducted in rabbits to assess skin irritation, and based on the corrosive results of the study a determination was made for eye irritation. The studies were conducted in compliance with GLP. The quality of the study is deemed as reliable without restrictions.

Repeated Dose- This endpoint has not been determined and will be tested using OECD 422 to satisfy the SIDS requirement.

Genetic Toxicity Mutation- This endpoint is filled with data from a study that followed OECD Test Guideline 471 and was conducted under GLP regulations. This study utilized Salmonella typhimurium strains TA98, TA100, TA1535 and TA1537 in the presence and absence of a metabolic activation system. The quality of this study was deemed as reliable without restrictions.

Mouse Micronucleus Assay- This endpoint has not been determined and will be tested using OECD 474 to satisfy the SIDS requirement.

Reproductive Toxicity- This endpoint has not been determined and will be tested using OECD 422 to satisfy the SIDS requirement.

Developmental Toxicity- This endpoint has not been determined and will be tested using OECD 422 to satisfy the SIDS requirement.

Conclusion- Acute toxicity and gene mutation SIDS endpoints have been satisfied from existing studies. Testing will be conducted to satisfy those SIDS endpoints which have not been filled. The Repeat Dose Toxicity, Reproductive/Developmental Toxicity

endpoints will be satisfied by conducting testing using OECD 422. Combining the testing in a single protocol will require the use of fewer animals.

SIDS DATA SUMMARY

Data determining the density was obtained from actual testing using a densitometer. A value of 0.7698 g/cc was measured. Data determining the partition coefficient was obtained from actual testing by the shake flask method. A log P of 1.09 $\pm$ 0.20 was calculated. Data determining the dissociation constant was obtained using Potentiometric titration in non-aqueous solvent to determine the Half Neutralization Potential because the test substance was not sufficiently water soluble. From this, the pK_a value of 10.5 was estimated.

The AOP Model v 1.91 resident within EPIWIN was used to estimate atmospheric degradation of Primene™ TOA. For hydroxyl radical reactions AOPWIN estimated the hydrogen abstraction rate constant to be 2.25E-12 cm^3/molecule-sec. The reaction rate with N, S, and –OH was estimated to be 21.0E-12 cm^3/molecule-sec. The overall OH radical rate constant was estimated to be 23.25E-12 cm^3/molecule-sec. The estimated half-life equaled 5.52 hours assuming a 12 hour day and 1.5E06 OH/cm^3. The model was unable to estimate ozone reaction kinetics because no structurally similar molecules were within the database.

HYDROWIN was unable to estimate hydrolysis rate constant because no similar chemical structures are in the database.

The Level I fugacity model calculates the distribution of a fixed quantity 1.0E05 kg of a conserved, i.e., non-reacting chemical in a closed environment at equilibrium, with no degrading reactions, no advective processes and no intermedia transport. The medium receiving the emission is unimportant because the chemical is assumed to become instantaneously distributed.

The Level III Fugacity model calculates the steady state distribution of a chemical, in an environment not at equilibrium. The chemical is continuously discharged at a constant rate, 1000 kg/hr, into the chosen environmental media, and achieves a steady-state condition at which input and output rates are equal. This involves calculating the rates of degradation and advection, from half-lives or rate constants, and advective flow rates and considering the emission. Intermedia transport processes (e.g. wet deposition, evaporation, or sedimentation) are included. The media receiving the emissions are very important and have a controlling influence on the overall fate of the chemical.

The environmental fate parameters used in determining the fugacity of Primene™ TOA were derived using EPIWIN v 3.12 and include:

Molecular weight: 129.25
Water Solubility: 10670 (mg/L)
Vapor pressure: 8.03 mm Hg, 1070.58 Pa (estimated using MPBPWIN)

Log Kow: 2.58 (estimated using KOWWIN)
Melting Point: -20.02 (estimated using MPBPWIN)
Half-lives (h):
Air: 11
Water: 900
Soil: 1.8E03
Sediment: 8.1E03

The half-lives in the environmental media were generated using the Level III fugacity model resident in EPIWIN employing the estimated environmental fate parameters. The Level III fugacity model resident within EPIWIN is based on the EQC model. The advantage of using the stand alone model is that it can be parameterized to generate Level I, II or III output.

The following table illustrates the percentage of the chemical in the air, water, soil and sediment compartments based on Level I output.

Table 1. Level I EQC Fugacity Model Compartmental Mass Distribution

Compartment	Mass (percent)	Half-life (hr)
Air	66.1	11
Water	25.3	900
Soil	8.50	1.8E03
Sediment	0.189	8.1E03

Level III output are illustrated in the following table:

Table 2. Level III EQC Fugacity Model Compartmental Mass Distribution

Compartment	Mass (percent)
Air	1.02
Water	19.7
Water: Fish	3.74E-04
Soil	79.1
Sediment	0.187

For the Level III fugacity modeling, continuous discharge of 1000 kg/hour into the air, water and soil compartments was assumed. Partitioning into the sediment compartment was driven by adsorption kinetics. The reaction rate kinetics were estimated to decrease in air, water and soil, respectively. The fugacity parallels this relationship where the atmosphere would serve as the primary "sink" for Primene™ TOA followed by the water compartment, sediment and soil. Based on half-lives and environmental fate characteristics Primene™ TOA would be anticipated to compartmentalize predominantly in the soil (79.1% of the entire mass) and aquatic compartments (19.7% of the entire mass), with lesser mass percentages in biota, air and sediments.

Primene^{TM} TOA is considered moderately toxic following acute oral exposure. The oral LD_{50} of male and female rats (combined) was 217.7 mg/kg. Signs of apparent neurotoxicity were observed in rats treated with up to 500 mg/kg by gavage. Data from a skin irritation study in rabbits indicates that Primene^{TM} TOA is corrosive to the skin, and thus the eye.

Results from a mutagenicity study indicate that Primene^{TM} TOA was not mutagenic in an Ames mutagenicity assay using Salmonella typhimurium with or without metabolic activation.

EVALUATION OF DATA FOR QUALITY AND ACCEPTABILITY

The collected data were reviewed for quality and acceptability following the general US EPA guidance and the systematic approach described by Klimisch *et al.* (1997). These methods include consideration of the reliability, relevance and adequacy of the data in evaluating their usefulness for hazard assessment purposes. This scoring system was only applied to human health endpoint studies per EPA recommendation. The codification described by Klimisch *et al.* (1997) specifies four categories of reliability for describing data adequacy. These are:

(1) Reliable without restriction: Includes studies or data complying with Good Laboratory Practice (GLP) procedures, or with valid and/or internationally accepted testing guidelines, or in which the test parameters are documented and comparable to these guidelines.
(2) Reliable with restriction: Includes studies or data in which test parameters are documented but vary slightly from testing guidelines.
(3) Not reliable: Includes studies or data in which there are interferences, or that use non-relevant organisms or exposure routes, or which were carried out using unacceptable methods, or where documentation is insufficient.
(4) Not assignable: Includes studies or data in which insufficient detail is reported to assign a rating, e.g., listed in short abstracts or secondary literature (books, reviews, etc.)

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